

USSN: 09/392,822

Current claim set after amendment (Claims 1,8,14-16, 21, 24-26, 32-46 are pending)

1. (amended) A replication-competent adenovirus vector for selective cytolysis of a target cell comprising,
a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1.
8. (restated) The adenovirus vector of claim 1, wherein the HRE is human.
14. (restated) The adenovirus vector of claim 1, wherein said adenovirus gene essential for replication is operably linked to a composite regulatory element comprising said HRE and a tumor cell-specific transcriptional regulatory element (TRE).
15. (restated) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises a promoter.
16. (restated) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises an enhancer.
21. (restated) The adenovirus vector of claim 14, wherein said tumor cell-specific TRE comprises a prostate specific promoter and enhancer.
24. (amended) A composition comprising:
a replication-competent adenovirus vector for selective cytolysis of a target cell comprising a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1; and
a pharmaceutically acceptable excipient.
25. (restated) An isolated host cell comprising the adenovirus vector of claim 1.
26. (restated) A method of propagating adenovirus *in vitro*, the method comprising:
introducing into a cell an adenovirus vector comprising a hypoxia responsive element (HRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4, wherein said HRE comprises a binding site for hypoxia inducible factor-1 wherein said cell is maintained under hypoxic conditions *in vitro*, thereby expressing said adenovirus gene essential for replication;
wherein said adenovirus is propagated.
32. (restated) The method of Claim 26, wherein said propagating of said adenovirus is cytotoxic to said cell.
33. (restated) The method of Claim 32, wherein said cell is a tumor cell.

USSN: 09/392,822

34. (restated) The adenovirus vector of claim 14, wherein said tumor cell-specific transcriptional regulatory element (TRE) is selected from the group consisting of a prostate-specific TRE (PSA-TRE), a glandular kallikrein-1 TRE (*hKLK2*-TRE), a probasin TRE (*PB*-TRE), an α -fetoprotein TRE (AFP TRE) and a carcinoembryonic antigen TRE (CEA TRE).

35. (restated) A replication-competent adenovirus vector for selective cytolysis of a target cell, comprising:

an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4.

36. (restated) The adenovirus vector of claim 35, wherein the E2F-1 TRE is human.

37. (restated) The adenovirus vector of Claim 36, wherein said E2F-1 TRE comprises the nucleotide sequence set forth in SEQ ID NO:2.

38. (restated) The adenovirus vector of Claim 35, wherein said E2F-1 TRE comprises a nucleotide sequence having at least 80% sequence identity with the sequence set forth in SEQ ID NO:2.

39. (restated) The adenovirus vector of Claim 35, wherein said E2F-1 TRE comprises a nucleotide sequence that hybridizes under stringent conditions with the sequence set forth in SEQ ID NO:2.

40. (restated) The adenovirus vector of Claim 35, wherein said adenovirus gene essential for replication is operably linked to a composite regulatory element comprising said E2F-1 TRE and a tumor cell-specific transcriptional regulatory element (TRE).

41. (restated) The adenovirus vector of claim 40, wherein said tumor cell-specific transcriptional regulatory element (TRE) is selected from the group consisting of a prostate-specific TRE (PSA-TRE), a glandular kallikrein-1 TRE (*hKLK2*-TRE), a probasin TRE (*PB*-TRE), an α -fetoprotein TRE (AFP TRE) and a carcinoembryonic antigen TRE (CEA TRE).

42. (restated) A composition comprising:

a replication competent adenovirus vector for selective cytolysis of a target cell, comprising an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4; and

a pharmaceutically acceptable excipient.

43. (restated) An isolated host cell comprising the adenovirus vector of Claim 35.

44. (restated) A method of propagating adenovirus *in vitro*, the method comprising:

a replication competent adenovirus vector for selective cytolysis of a target cell, comprising an E2F-1 transcriptional regulatory element (TRE) operably linked to an adenovirus gene essential for replication selected from the group consisting of E1A, E1B and E4 wherein said cell is maintained under cell cycling conditions *in vitro*, thereby expressing said adenovirus gene essential for replication;

USSN: 09/392,822

wherein said adenovirus is propagated.

45. (restated) The method of Claim 44, wherein said propagating of said adenovirus is cytotoxic to said cell.

46. (restated) The method of Claim 44, wherein said cell is a tumor cell.